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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/080,503	02/22/2002	Robert I. Higuchi	015110.0058.UTL1	8671
36183	7590	01/25/2006	EXAMINER	
PAUL, HASTINGS, JANOFSKY & WALKER LLP			CRANE, LAWRENCE E	
P.O. BOX 919092			ART UNIT	PAPER NUMBER
SAN DIEGO, CA 92191-9092			1623	

DATE MAILED: 01/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/080,503

Applicant(s)

HIGUCHI ET AL.

Examiner

L. E. Crane

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on November 3, 2005 (amdt).  
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☐ Claim(s) 1-31, 37-42, 46, 49-51, 56-72 and 75-77 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
5) ☒ Claim(s) 56 and 57 is/are allowed.  
6) ☒ Claim(s) 1-31, 37-42, 46, 49-51, 58-72 and 75-77 is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.  
10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 09/09/2005.  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.  
5) ☐ Notice of Informal Patent Application (PTO-152)  
6) ☐ Other: \_\_\_\_\_.

Claims 32-36, 43-44, 47-48, 52-55, 73-74, and 80-107 have been cancelled, claims 1-7, 9, 11-18, 20-21, 23-31, 39, 41-42, 45, 49-51, 56-58, 60-72 and 76-77 have been amended, the disclosure has been amended, and no new claims have been added as per the amendment of November 3, 2005. A supplemental Information Disclosure Statement (IDS) filed September 9, 2005 has also been received with all cited foreign and NPL references and made of record.

Examiner notes that the listings above are slightly different from applicant's claim listings, but the above listings appear to correspond exactly to the actual claim status indicators in the November 3, 2005 amendment.

Note to applicant: when a rejection refers to a claim X at line y, the line number "y" is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Claims 1-31, 37-42, 45-46, 49-51, 56-72 and 75-77 remain in the case.

Claims 1-31, 37-42, 45-46, 49-51, 58-72 and 75-77 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention; the scope is excessive in view of the disclosed exemplifications.

The definitions of substituents in claim 1 is directed to a vast number of chemical compounds which have not been described in the instant disclosure in a manner permitting the ordinary practitioner to have the guidance necessary to make a very large proportion of the compounds encompassed. Examiner finds only about 150 compounds which are precursors, intermediates or final products (variously substituted [1,4]oxazino[2,3-f]quinolin-8-ones) provided in the "Examples" section. No other tricyclic ring nucleus has been disclosed as having been synthesized within the examples. And additionally none of the exemplary compounds discloses a structure with the multiple layers of substituents on top of substituents provided for by the noted claim or provides a complete description of how to make same.

Applicant is again respectfully requested to substantially narrow the scope of the instant generic and sub-generic claims to reflect the scope of the contribution actually made in light of the guidance provided below.

Applicant's arguments filed November 3, 2005 have been fully considered but they are not deemed to be persuasive.

Applicant has not yet responded with amendments to the criticisms concerning the functional language "optionally substituted." This failure means that the scope of the instant claims remains excessive. Examiner respectfully requests amendment of the claims to define what is meant by the noted term in each different location within the noted claims, deletion of the noted functional language or some combination thereof.

Claims **1-31, 37-42, 45-46, 49-51, 58-72 and 75-77** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the compound claims is excessive because of the presence of numerous Markush groups and nested Markush groups; see claim **1** in particular. In addition, the repeated use of the term "may be optionally substituted" without specifying the substituents implied thereby renders the breadth excessive because said term implies that the unnamed substituents is/are open to all possible alternatives.

B. The nature of the invention includes a method of testing, a method of purification, and a vast number of methods of medicinal treatment wherein compounds of instant claim **1** are administered to a host in need of said treatment. Claims **1-31, 37-42, 45-46, 49-51, 58-72 and 75-77** are directed to a vast array of compounds defined by a series of Markush groups and pharmaceutical compositions thereof.

C. The state of the prior art is defined by the prior art presently cited by applicant and by examiner and particularly by PTO-892 references **F and G** wherein anticipatory compounds and compositions have been disclosed.

D. The level of one of ordinary skill in the relevant chemical synthesis arts is high because the syntheses of many compounds very closely analogous to the instant claimed compounds are known in the art (PTO-892 references **F and G**). However, the level of one of ordinary skill in the medical arts is moderate because it is unclear which if any of the compounds disclosed herein are active against one or more specific disease conditions.

E. The level of predictability in the art is indeterminate in light of the instant disclosure wherein there is no clear showing that compounds which are active as androgen receptor agonists or antagonists are actually effective in the treatment of any specific disease condition. If applicant has additional art bearing on this question, examiner respectfully requests submission of same at applicant's earliest convenience.

F. The amount of direction provided by the inventor is limited to the chemical syntheses of numerous [1,4]oxazino[2,3-*f*]quinolin-8-ones and data identifying which compounds are antagonists and which are agonists in the presence of known androgen receptors. However, no other chemical species have been disclosed as having been synthesized, isolated, or subjected to any test regimen to determine possible medicinal activity.

G. The existence of working examples is limited to those noted in the previous section of this rejection.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive because the instant specification only discloses how to make compounds with a [1,4]oxazino[2,3-*f*]isoquinolin-8-one ring system, the 8-O-protected analogues, thereof and precursors prepared during the synthesis thereof. While applicant has shown that the compounds disclosed herein have potential utility in the treatment of disease conditions wherein an androgen-sensitive receptor has been implicated, there has been no showing that any particular disease condition may be effectively treated by administration of any single compound of claim 1 to any host, including cells in culture.

Applicant's arguments filed November 3, 2005 have been fully considered but they are not deemed to be persuasive.

Applicant is referred to the guidance following the previous rejection *supra*. The remainder of these remarks include a partial repetition of the previous response to applicant's argument in the last Office action.

The compound and pharmaceutical composition claims are only enabled in part because the instant claims include terms which are incomplete defined (aryl, arylalkyl, heteroaryl, etc.) because said terms typically

- i) lack any upper bounds as to size,
- and when hetero atoms are suggested said terms,
- ii) fail to define which hetero atoms are to be selected from,
- iii) the number of said hetero atoms, or
- iv) the location(s) or the ring system(s) containing said hetero atom(s), and
- v) because a proper definition of "optionally substituted" is not present in any independent claim.

Examiner also notes that newly cited prior art (references **L, M & N**), which cannot be cited in an art rejection but which is very close, implicates the parts of the instant claims wherein spiro structures are claimed (e.g.: "R<sup>3</sup> and R<sup>4</sup> taken together form a three to eight membered saturated or unsaturated carbocyclic or heterocyclic ring," etc., etc.). Examiner has not found any heterocyclic or homocyclic spiro examples in any of the seven illustrated synthetic schemes or any of the compounds specifically reported by the disclosure. Again examiner refers applicant to the teachings of *Brenner v. Manson* *supra* and respectfully requests additional disclosure in the form of declaration evidence and a noticeable narrowing in part by definitional improvement of the claims.

In addition examiner suggests that the definitions of variables "X" and "Z" should be separated because, in light of the fact that "W" is the "nitrogen" of the oxazine ring, then "X" must always be the "O" of said ring. Examiner also suggests that the definition of "W" should be limited to "substituted nitrogen moieties" in light of the scope of the specific embodiments.

In summary, applicant is encouraged to further narrow and refine the scope of the instant claims.

Claims 1-3, 5-7, 9, 11-18, 20-21, 23, 25, 27, 29-30, 49, 58, 60-62, 64-71 and 73-74 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1-3, 5-7, 9, 11-18, 20-21, 23, 25, 27, 29-30, 49, 58, 60-62, 64-71 and 73-74 the term “optionally substituted” is incomplete for failure to specify the substituents implied thereby. See also claims 4, 22, 24 and 28 wherein the term “optionally substituted” continues to have the same problem, mk.

Applicant’s arguments filed November 3, 2005 have been fully considered but they are not deemed to be persuasive.

Applicant is referred to examiner’s comments following the first rejection supra. The following is a repetition of examiner’s remarks from the last Office action.

Examiner notes that the all encompassing terms at the end of the definition of many variable with claim that various listed groups “.. may be optionally substituted” has been deleted in favor of the selective use of the term “optionally substituted” except in the case of “C<sub>1-8</sub> alkyl” in the definition of variable R<sup>18</sup> in claims 1 and 58. Careful inspection of the Marui patents suggests that compounds including the substituent group “-CH<sub>2</sub>-OH” have thereby been avoided. Anyone reading the original or the amended claims or both would not have otherwise known that “hydroxyl” was an “optional substituent.” For this reason examiner suggests that the term “optionally substituted” should be specifically defined in the independent claims (claims 1 and 58).

Applicant’s argument that the definition found in the disclosure is adequate is found to be inadequate because the quoted definition fails to meet the requirements of the statute for a variety of reasons noted in examiner’s response following a previous rejection.

Claims 56 and 57 are allowable as amended herein.

Claims 1-31, 37-42, 45-46, 49-51, 58-72 and 75-77 would be allowable if rewritten or amended to overcome the rejection under 35 U.S.C. §112.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

A shortened statutory period for response to this final action is set to expire **THREE MONTHS** from the date of this action. In the event a first response is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than **SIX MONTHS** from the date of this final action.

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 703-872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

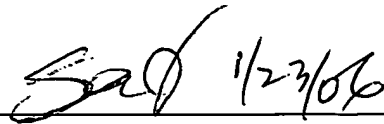
Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.



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01/23/2006



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